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Meta-Analysis

Comparison of oral and intravenous iron for the prevention and management of iron deficiency anaemia in pregnancy: a systematic review and meta-analysis

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ABSTRACT

Iron-deficiency anaemia (IDA) affects nearly 38% of pregnant women worldwide and is linked to maternal complications and poor birth outcomes. Although oral iron is the standard treatment, its use is often limited by gastrointestinal side effects and poor adherence. Intravenous (IV) iron may offer faster and better-tolerated correction of anaemia. This systematic review and meta-analysis compared IV and oral iron for the prevention and management of IDA in pregnancy. This review was registered with PROSPERO and conducted according to PRISMA guidelines. A total of 4,216 articles were screened, and 17 eligible studies, including 16 randomized controlled trials, were included. Two reviewers independently performed data extraction and quality assessment. Random-effects meta-analysis using the DerSimonian and Laird method was conducted. Primary outcomes were haemoglobin and serum ferritin; secondary outcomes included maternal and neonatal outcomes and treatment-related adverse events. IV iron produced significantly greater improvements in haemoglobin (mean difference 0.7 g/dl; 95% CI: 0.4-1.0) and serum ferritin (mean difference 79.4 ng/ml; 95% CI: 21.8-137) than oral iron. The odds of maternal anemia were reduced by 71% with IV therapy (OR 0.29; 95% CI: 0.08-1.00). No significant differences were observed in cord haemoglobin or cord ferritin, although ferritin showed a favourable non-significant trend. Adverse events were less frequent with IV iron, but the difference was not statistically significant. IV iron was more effective than oral iron in improving haematological outcomes in pregnant women with IDA and may be preferred in moderate-to-severe anemia, oral iron intolerance, or late gestation.

Keywords: Iron-deficiency anemia, Pregnancy, Intravenous iron, Oral iron, Randomized controlled trials

INTRODUCTION

Iron deficiency anaemia (IDA) is the most prevalent micronutrient deficiency in pregnancy, affecting an estimated 38% of pregnant women globally, with the burden disproportionately higher in South Asia and Sub-Saharan Africa.[1] In India alone, the prevalence of anaemia among pregnant women is estimated to be over 50%, according to the National family health survey (NFHS-5).[2] The increased iron requirement during pregnancy, nearly 1000 mg of additional iron, is driven by expansion of maternal blood volume, foetal growth, and placental development.[3] Iron supplementation plays a critical role in safeguarding both maternal and foetal health. Untreated IDA during pregnancy has been associated with increased risks of preterm birth, low birth weight, intrauterine growth restriction, and perinatal mortality.[4,5] On the maternal side, it increases susceptibility to infections, impairs physical and cognitive performance, causes

fatigue, and elevates the risk of postpartum haemorrhage and maternal mortality.[6]

Oral iron supplementation has long been the standard approach, supported by WHO and national guidelines for preventing and treating mild to moderate anaemia during pregnancy.[7] However, the effectiveness of oral iron is often compromised by poor gastrointestinal tolerance, non-compliance, and delayed haemoglobin response, particularly in cases of moderate to severe anaemia or late antenatal booking.[8]

Intravenous (IV) iron has demonstrated superior efficacy compared to oral iron in achieving faster and more substantial increases in haemoglobin levels and replenishment of iron stores, especially in moderate to severe anaemia and in late pregnancy where time to delivery is limited.[9,10] Studies have shown that IV iron, particularly newer formulations such as ferric carboxymaltose (FCM) and iron sucrose, leads to a greater and quicker increase in haemoglobin concentration and serum ferritin within 2–3 weeks of administration.[10]

A multicentre randomised controlled trial by Breymann et al reported that IV iron sucrose increased haemoglobin levels by 2.1 g/dl in 4 weeks, compared to 1.3 g/dl with oral iron.[11] Similarly, Qassim et al, in a meta-analysis found that IV iron had a statistically significant greater increase in haemoglobin levels at 4 and 8 weeks, with fewer treatment failures compared to oral therapy.[12]

Despite growing evidence, clinical uncertainty remains regarding the optimal modality, timing, and population subset for intravenous versus oral iron therapy. A focused meta-analysis comparing the efficacy, safety, and outcomes of oral and intravenous iron in pregnancy will help refine clinical guidelines and contribute to better maternal and neonatal health outcomes.

METHODS

This systematic review and meta-analysis was conducted at Bloom IVF Centre, Lilavati Hospital and Research Centre, Mumbai, India, between April 2025 and August 2025, in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines.[13] The study protocol was developed and prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO) under the registration number (CRD420251088669), in accordance with established methodological standards to ensure transparency, reproducibility, and minimisation of reporting bias.[14]

Search strategy and eligibility criteria

A comprehensive electronic literature search was conducted using five major databases: PubMed/MEDLINE, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), Scopus, and CINAHL. Grey literature sources were also searched, including ClinicalTrials.gov and the WHO International clinical trials registry platform (ICTRP). In addition, we conducted manual searching of the reference lists of included studies and relevant review articles to ensure completeness.[15]

The search strategy was constructed using a combination of medical subject headings (MeSH) and free-text terms, including “iron deficiency anaemia,” “pregnancy,” “oral iron,” “intravenous iron,” “ferrous sulfate,” “ferric carboxymaltose,” and “maternal anaemia.” Boolean operators (“AND” and “OR”) were used to appropriately combine terms. The search strategy was peer-reviewed using the PRESS (Peer review of electronic search strategies) 2015 checklist to ensure clarity and comprehensiveness.[16] The complete search strategy for each database is provided in Supplementary Table 1.

Eligibility criteria were defined using the PICO framework. We included randomised controlled trials (RCTs), cohort/comparative studies, systematic reviews and meta-analys is that compared intravenous iron therapy with oral iron supplementation in pregnant women. Eligible participants were pregnant women at any gestational age, diagnosed with or at risk for Iron deficiency anaemia (IDA). The operational definition of anemia during pregnancy was defined according to the World Health Organization (WHO) as a haemoglobin concentration below 11 g/dl during pregnancy.[17]

Interventions of interest included any form of intravenous iron, such as iron sucrose, ferric carboxymaltose, or iron dextran. The comparator was oral iron supplementation, including formulations like ferrous sulphate or ferrous fumarate. Studies were required to report at least one relevant outcome: haematological parameters (haemoglobin, serum ferritin, transferrin saturation), maternal and foetal outcomes (birth weight, gestational age at delivery, Apgar score), adverse events (e.g., gastrointestinal intolerance, allergic reactions), need for blood transfusion, or adherence/compliance rates.

Studies published in English between January 2005 and July 2025 were considered. We excluded non-comparative studies, reviews, editorials, letters, case reports, conference abstracts without full-text data, and studies involving postpartum anemia or non-pregnant populations. We excluded studies if the mean and standard deviation for continuous outcomes related to hematological, maternal, or fetal parameters were not reported, or if only change from the baseline values were provided without exact measurements.

All retrieved citations were checked for deduplication. Two reviewers independently screened titles and abstracts for eligibility. Full texts of all included articles on title and abstract screening were retrieved and reviewed against the inclusion criteria. Discrepancies in both title and abstract

screening and full-text screening were resolved through discussion or consultation with a third reviewer. The selection process was documented using a PRISMA 2020 flow diagram.[13]

Data extraction

Data were extracted independently by two reviewers using a standardised, pre-tested data extraction form in excel. The form collected information on study characteristics (authors, year, country, design), participant demographics (age, gestational age, baseline haemoglobin), details of the intervention and comparator (formulation, dosage, frequency, duration), and all eligible stated outcomes. When necessary, third reviewer was contacted to clarify or supplement reported data. Disagreements were resolved by consensus.[18]

Risk of bias assessment

Two authors independently critically appraised the included studies which involved assessing the methodological rigor of each study and determining how effectively potential biases were addressed in its design, conduct, and analysis. We applied the Joanna Briggs Institute (JBI) Critical appraisal checklists for cohort studies (Joanna Briggs Institute, 2017) and randomised controlled trials (RCTs).[19] The JBI checklist for cohort studies (11 items) covers group comparability, exposure, confounders, outcomes, follow-up, and statistics. The RCT checklist (13 items) addresses randomisation, blinding, group comparability, outcomes, follow-up, and statistical analyses (Joanna Briggs Institute, 2017). Each appraisal item was scored as "yes," "no," or "unclear" with two points assigned for "yes", one point for "unclear" and zero for "no". The review's overall assessment of bias for the study considered all the aspects to arrive at the final classification of low/moderate/high risk of bias.

Data synthesis and statistical analysis

We performed meta-analyses using Review manager (RevMan) version 5.4 and RStudio version 4.4 using the meta and metaphor packages. For continuous outcomes such as and ferritin levels, we calculated Mean differences (MD) or Standardised mean differences (SMD) with 95% Confidence intervals (CIs). For dichotomous outcomes such as adverse events and transfusion rates, we calculated Odds ratios (OR) with their 95% CIs.

A random-effects model was employed using the Der Simonian and Laird method to account for expected clinical and methodological heterogeneity, regardless of statistical evidence of heterogeneity.[22] Forest plots were generated to visually represent pooled effect sizes with its 95% CI. Sensitivity analysis was performed for outcomes with more than 10 papers by removing papers with high risk on bias. For outcomes with ≥10 studies available, funnel plots were made to visualize publication bias, and Egger's test was performed to statistically evaluate funnel plot symmetry.

RESULTS

A total of 4,216 records were identified through database searching. After removing 3,920 duplicate records, 296 records were screened by title and abstract. Of these, 151 were excluded for reasons such as absence of IV iron, observational design, non-pregnant populations, or lack of relevant outcomes. Subsequently, 141 full-text articles were assessed, with 110 meeting the inclusion criteria for qualitative synthesis. Among these, twenty-six studies comprising RCTs, cohort studies, meta-analysis and systematic review were included in the analysis, and 17 contributed to the primary comparison of intravenous versus oral iron. The study selection process is summarised in the PRISMA flow chart (Figure 1).

The characteristics of the included studies are summarized in Table 1. Among all, 17 were randomised controlled trials and one was cohort study involving pregnant women diagnosed with iron deficiency anaemia. Sample sizes varied across studies. The intravenous iron formulations used were primarily iron sucrose, ferric carboxymaltose, and iron dextran, while oral iron preparations commonly included ferrous sulfate and ferrous fumarate. Key outcomes assessed across the studies included haematological parameters such as haemoglobin and serum ferritin levels, maternal and fetal outcomes, and adverse events.

Outcomes

Maternal hemoglobin and serum ferritin levels

15 and 7 of total 17 measured pre- and post- intervention hemoglobin levels (g/dl) and serum ferritin levels (ng/ml) respectively. For haemoglobin levels, the pooled mean difference was 0.7 (95% CI: 0.4 to 1.0), indicating that the intravenous group had significantly higher haemoglobin levels compared to the oral group (Figure 2). The effect sizes among individual studies ranged from -0.1 to 1.9, with studies like Tondge et al and Dura et al reporting the largest mean differences in favour of intravenous treatment.[28,20] For serum ferritin, the pooled mean difference was 79.4 (95% CI: 21.8 to 137), also indicating that the intravenous group had significantly higher ferritin levels compared to the oral group (Figure 3). The effect sizes among individual studies ranged from 3.5 to 234.7, with Chauhan et al reporting the largest mean difference in favour of intravenous treatment.[23,29]

Both the outcomes had I^2 of >90.0%, suggesting considerable variability not attributable to random chance, and heterogeneity test was statistically significant ($p<0.001$). Weight distribution across studies was fairly uniform, ranging between 5.0% and 7.1% for hemoglobin levels and 12.0% and 14.8% for serum ferritin levels, suggesting a uniform weightage across studies. The forest

plot in Figure 2 and 3 presents the individual and pooled estimates of MD, along with their 95% CI for hemoglobin levels and serum ferritin levels respectively. The funnel plot for maternal haemoglobin level outcome did not show asymmetry, confirmed with non-significant Egger test (p value=0.94) indicating no evidence of publication bias.

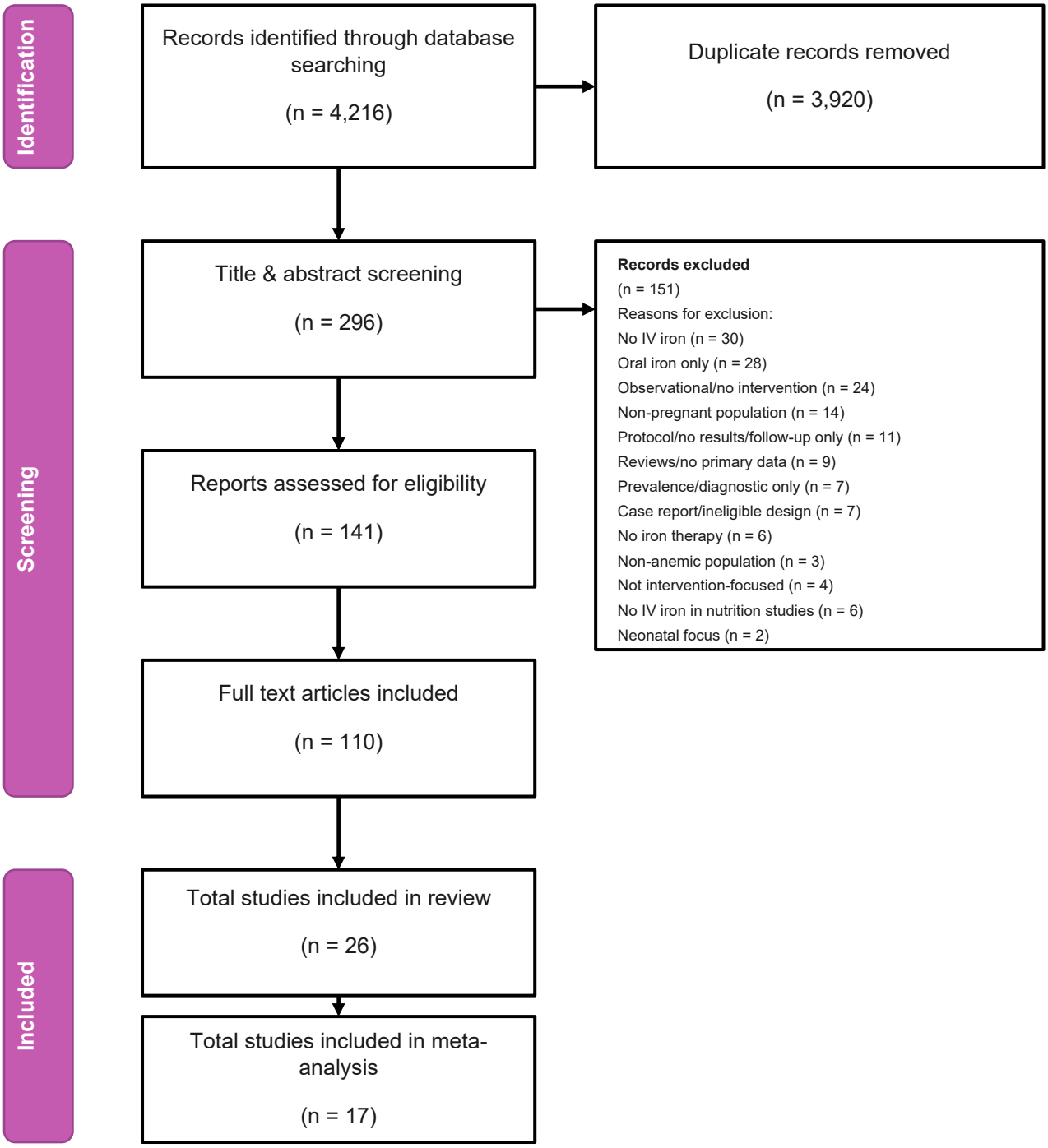

Figure 1: PRISMA flow chart.

Maternal anemia

For maternal anemia, forest plot in Figure 4 illustrates the OR with corresponding 95% CI for five studies. The pooled odds ratio was 0.29 (95% CI:0.08 to 1.00), suggesting that the intervention group had a 71% reduction in odds of maternal anemia compared to the control group. However, the upper bound of the confidence interval reaches 1.00, indicating borderline statistical significance. Lewkowitz et al.[23] (OR:0.12, 95% CI: 0.02-0.87) and

Chawla et al, (OR: 0.04, 95% CI: 0.01-0.09) reported the most pronounced protective effects of the intervention. Conversely, Afolabi et al showed an OR close to unity (OR:0.89, 95% CI:0.69-1.14), indicating no significant difference between groups.[25] Heterogeneity was high, with an I^2 of 92.9%, indicating considerable between-study variability. The between-study variance was quantified as τ^2=1.7693, and the test for heterogeneity was highly significant (p<0.001).

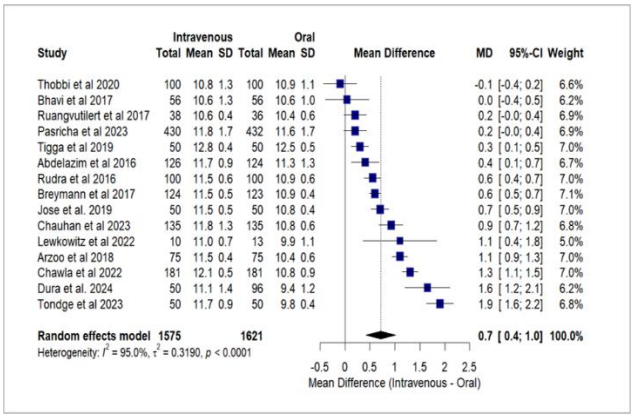

Figure 2: The forest plot shows the average haemoglobin (g/dl) levels in pregnant subjects who received IV iron vs. oral iron.

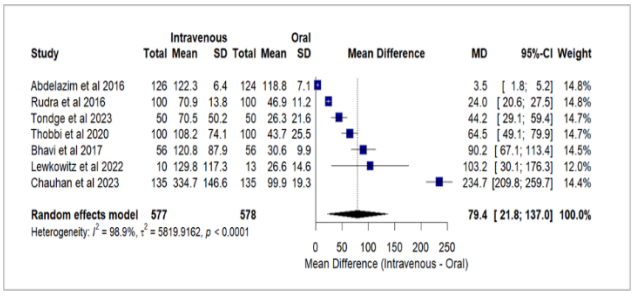

Figure 3: The forest plot shows the average serum ferritin (ng/ml) levels in pregnant subjects who received IV iron vs. oral iron.

Newborn cord hemoglobin and serum ferritin levels

Three studies had newborn cord hemoglobin and serum ferritin levels as outcomes. For newborn cord hemoglobin, the pooled mean difference was -0.1 (95% CI: -0.4 to 0.2), indicating no statistically significant difference between the intravenous and oral groups. The confidence interval crosses zero, suggesting no clear superiority of either treatment method. Individual study estimates also reflect small differences. Khalafallah et al reported a mean difference of -0.5 (95% CI: -1.3 to 0.3), Rudra et al, observed -0.2 (95% CI:-0.4 to 0.0), and Breymann et al showed a slight positive difference of 0.2 (95% CI:-0.3 to 0.7), none of which reached statistical significance.[9,26,36]

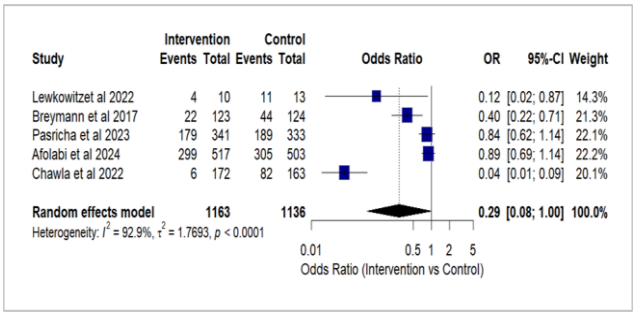

Figure 4: The forest plot shows odds of maternal anemia in pregnant subjects between those who received IV iron vs. oral iron.

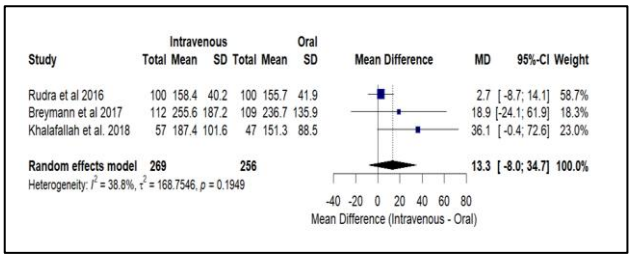

Figure 5: The forest plot shows the average newborn cord serum ferritin levels in pregnant subjects who received IV iron vs. oral iron.

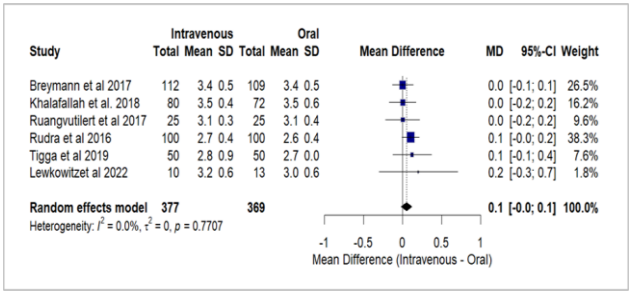

Figure 6: The forest plot shows the average newborn weight in pregnant subjects who received IV iron vs. oral iron.

For newborn cord serum ferritin, the pooled mean difference was 13.3 (95% CI:-8.0 to 34.7), indicating a trend towards higher levels of newborn cord serum ferritin in the intravenous group compared to the oral group. However, the confidence interval is wide and crosses zero, suggesting that this difference is not statistically significant. Individually, Rudra et al, reported a small mean difference of 2.7 (95% CI:-8.7 to 14.1), while Khalafallah et al, observed a larger, though non-significant, mean difference of 36.1 (95% CI: -0.4 to 72.6).[35] Breymann et al also indicated a positive effect, but with wide uncertainty (MD:18.9 (95% CI:-24.1 to 61.9) (Figure 5).[9]

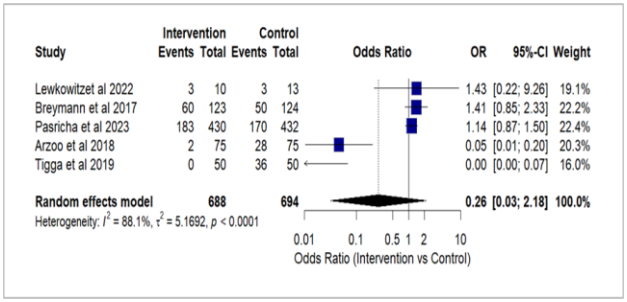

Figure 7: The forest plot shows the odds of adverse events in pregnant subjects who received IV iron vs. oral iron.

Heterogeneity among the studies for both outcomes was low to moderate, and a non-significant heterogeneity test. Figure 5 presents the forest plots for the newborn cord serum ferritin.

Newborn weight

The overall pooled mean difference from six included studies that assessed this outcome was 0.1 (95% CI:-0.0 to 0.1), indicating a negligible and statistically non-significant difference between the intravenous and oral groups (Figure 6). Across all included studies, the mean difference estimates were very close to zero, with none of the individual confidence intervals excluding the null value. Heterogeneity among the studies was negligible, as evidenced by an I^2 of 0.0%, τ^2=0, and a non-significant Cochran's Q test (p=0.771). This indicates consistency across studies, with minimal between-study variability. Given the absence of heterogeneity, the random-effects model provided results similar to a fixed-effect model but was chosen to maintain consistency in analytical approach across analyses. The study Rudra et al, contributed the most weight (38.3%) to the pooled estimate due to its relatively larger sample size and smaller variance.[35]

Adverse events of intervention

For adverse events, five studies had reported the outcomes, displayed as a forest plot (Figure 7). The pooled odds ratio was 0.26 (95% CI:0.03 to 2.18), indicating a lower odd of adverse event in the intervention group compared to control, though the confidence interval is wide and crosses the null value, suggesting statistical non-significance. Among individual studies, Arzoo et al (OR:0.05 (0.01;0.20)) and Tigga et al (OR:0.00 (0.00; 0.07)) reported substantial reductions in the odds of adverse events with the intervention.[34,36] In contrast, Lewkowitz et al, Breymann et al, and Pasricha et al, had odds ratios favoring the intervention but with wide CIs that did not reach statistical significance.[9,21,23] Substantial heterogeneity was observed with an I^2 of 88.1%, τ^2=5.169, and a highly significant Cochran's Q test (p<0.001), indicating considerable between-study variability.

Risk of bias

Of the included studies, 16 were assessed using the JBI checklist for randomised controlled trials, and one study, Dura et al, was assessed using the JBI checklist for cohort studies.[20] Most studies demonstrated strong methodological quality in domains related to outcome measurement and clarity of study objectives, and shortcomings were observed in areas such as handling of confounding factors, blinding procedures, and follow-up adequacy. Overall, all included studies were rated as low risk of bias (Figure 8 and 9).

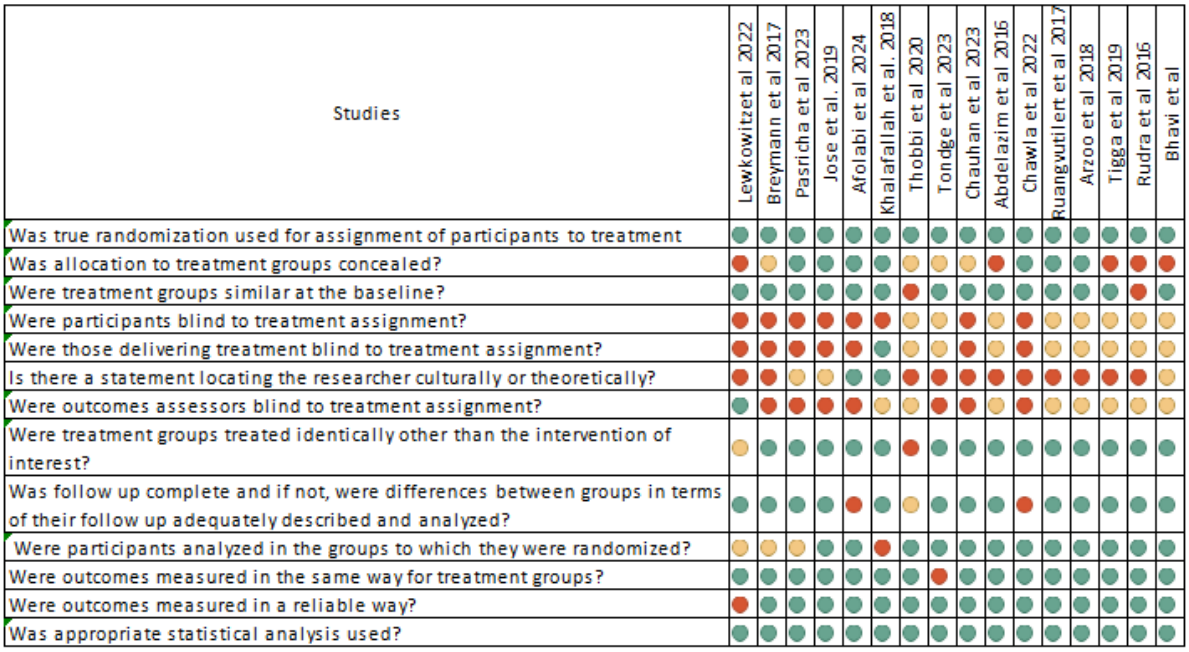

Figure 8: Risk of bias.

Study	Dura et al. 2024
1. Were the two groups similar and recruited from the same population?	
2. Were the exposures measured similarly to assign people to both exposed and unexposed groups?	
3. Was the exposure measured in a valid and reliable way?	
4. Were confounding factors identified?	
5. Were strategies to deal with confounding factors stated?	
6. Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	
7. Were the outcomes measured in a valid and reliable way?	
8. Was the follow up time reported and sufficient to be long enough for outcomes to occur?	
9. Was follow up complete, and if not, were the reasons to loss to follow up described and explored?	
10. Were strategies to address incomplete follow up utilized?	
11. Was appropriate statistical analysis used?	

Figure 9: Risk of bias assessment for the cohort study.

Table 1: Summary of the included studies.

S. no.	Author	Study design	Intervention (IV iron)/sample size	Comparator (oral iron)/sample size	Outcome
1	Lewkowitz et al, (2022)[42]	RCT	Iron dextran/(10)	Ferrous sulfate/(13)	IV iron significantly reduced the rate of maternal anemia at delivery
2	Breymann et al, (2017)[9]	RCT	Ferric carboxymaltose/(123)	Ferrous sulfate/(124)	IV ferric carboxymaltose was significantly more effective and faster than oral iron in correcting anemia
3	Pasricha et al, (2023)[21]	RCT	Ferric carboxymaltose/(430)	Ferrous sulfate/(432)	IV ferric carboxymaltose was safe but showed no significant benefit over oral iron in reducing anemia or improving birthweights
4	Jose et al, (2019)[24]	RCT	Ferric carboxymaltose/(50)	Iron sucrose complex/(50)	Ferric carboxymaltose showed a significant Hb rise (29 g/l vs 22 g/l), better fatigue improvement, and required fewer visits than iron sucrose over 12 weeks.
5	Afolabi et al, (2024)[25]	RCT	Ferric carboxymaltose/(517)	Ferrous sulfate/(503)	IV ferric carboxymaltose was not superior to oral ferrous sulphate in reducing anemia at 36 weeks of gestation but was more effective in improving iron stores in pregnant women.
6	Dura et al, (2024)[20]	Cohort study	Ferric carboxymaltose/(50)	Iron/(96)	Intravenous ferric carboxymaltose significantly improved haemoglobin levels at delivery and reduced the need for postpartum blood transfusion compared to oral iron
7	Khalafallah et al, (2018)[26]	RCT	Ferric carboxymaltose/(83)	Ferrous sulfate/(81)	IV ferric carboxymaltose and iron polymaltose significantly improved Hb and ferritin levels in pregnant women with better tolerance than oral iron.
8	Thobbi et al, (2020)[27]	RCT	Iron sucrose/(100)	Ferrous ascorbate+ folic acid/(100)	IV iron sucrose showed significant improvement in Hb and ferritin levels than oral iron, with good safety and compliance.
9	Tondge et al, (2023)[28]	RCT	Iron sucrose/(50)	Ferrous fumarate+ iron/(50)	Intravenous iron sucrose significantly improved haemoglobin and serum ferritin levels compared to oral iron in pregnant women with iron deficiency anemia.
10	Chauhan et al, (2023)[29]	RCT	Iron sucrose/(135)	Ferrous sulfate+folic acid/(135)	Intravenous iron sucrose was more effective and better tolerated than oral ferrous sulfate in improving anemia during pregnancy.

Continued.

S. no.	Author	Study design	Intervention (IV iron)/sample size	Comparator (oral iron)/sample size	Outcome
11	Abdelazim et al, (2016)[30]	RCT	Iron saccharate complex (ferrosac)/(126)	Heme iron polypeptide (proferrin-ES)/(124)	Oral proferrin-ES was as effective and well-tolerated as intravenous iron saccharate in treating iron deficiency anemia during pregnancy.
12	Chawla et al, (2022)[31]	RCT	Ferric carboxymaltose/(181)	Ferrous sulfate/(181)	Ferric carboxymaltose was more effective than oral ferrous sulfate in increasing haemoglobin in pregnant women with iron deficiency anemia, with no safety concerns.
13	Ruangvutilert et al, (2017)[32]	RCT	Iron sucrose complex)/(38)	Ferrous fumarate/(36)	Weekly low-dose intravenous iron sucrose was more effective in replenishing iron stores but not superior to oral iron in raising haemoglobin in late pregnancy.
14	Arzoo et al, (2018)[33]	RCT	Iron sucrose/(75)	Ferrous sulfate/(75)	Intravenous iron sucrose was significantly effective and better tolerated than oral ferrous sulfate in treating iron deficiency anemia during late pregnancy.
15	Tigga et al, (2019)[34]	RCT	Iron sucrose/(50)	Ferrous sulfate/(50)	Intravenous iron sucrose was significantly effective and better tolerated than oral iron in treating anemia during pregnancy.
16	Rudra et al, (2016)[35]	RCT	Iron sucrose/(100)	Ferrous ascorbate/(100)	Intravenous iron sucrose was significantly more effective and faster in increasing haemoglobin and ferritin levels than oral iron in pregnant women with iron deficiency anemia, with fewer side effects.
17	Bhavi et al, (2017)[36]	RCT	Iron sucrose/(56)	Ferrous fumarate/(56)	Intravenous iron sucrose significantly improved haemoglobin and ferritin levels more effectively than oral ferrous fumarate in pregnant women with iron deficiency anemia.

DISCUSSION

This systematic review and meta-analysis including 17 studies, evaluated the comparative efficacy, safety, and adherence of oral versus IV iron supplementation in pregnant women with or at risk of IDA. The pooled findings indicate that IV iron leads to significantly greater improvements in haematological parameters particularly haemoglobin and serum ferritin compared to oral iron. Specifically, haemoglobin levels were on average 0.7 g/dl higher in the IV group (95% CI:0.4-1.0), which corresponds to an approximate 7% relative improvement over oral iron. Similarly, serum ferritin levels were 79.4 ng/ml higher with IV iron, reflecting increase in iron stores relative to typical oral group values.

These findings are consistent with prior meta-analyses, which have highlighted IV iron's superiority in correcting anaemia and rapidly restoring iron reserves, particularly in women with moderate-to-severe anaemia or those requiring faster recovery.[37] The advantage of IV therapy is largely attributable to its ability to bypass gastrointestinal absorption, which is often impaired during pregnancy due to hormonal influences, inflammation, or poor tolerance to oral preparations.

In terms of maternal outcomes, IV iron was associated with a 71% reduction in the odds of maternal anaemia at delivery, suggesting meaningful clinical benefit. Although fetal outcomes were inconsistently reported, some studies indicated favourable trends with IV iron, including higher newborn cord haemoglobin and serum ferritin levels, and reduced risk of low birth weight. However, pooled analysis showed no statistically significant difference between groups for cord haemoglobin and birth weight, while cord ferritin levels were on average 13.3 ng/ml higher in the IV group, reflecting a trend toward improved neonatal iron status. Beyond efficacy, IV iron was better tolerated and achieved higher adherence compared to oral therapy. Gastrointestinal side effects common with oral iron, such as nausea, constipation, and metallic taste were markedly reduced with IV administration. The pooled odds ratio for adverse events was 0.26 (95% CI: 0.03-2.18), indicating lower risk in the IV group. Although infusion-related reactions were occasionally reported, they were generally

mild and self-limiting, with serious hypersensitivity events remaining rare.

Our findings are supported by existing evidence. Meta-analyses by Rogozinska et al and Govindappagari et al highlight the clinical benefits of IV formulations—particularly iron sucrose, and more recently ferric carboxymaltose, which allows larger doses to be administered in fewer sittings.[38,39] However, some caution has been raised by Qassim et al, who demonstrate current evidence does not unequivocally establish IV iron as a superior first-line therapy, emphasising that observed differences may be modest and influenced by study-level bias.[40]

It is important to note that the included trials exhibited variability in iron formulation, dosage, and frequency of administration, reflecting real-world clinical practice where therapy is highly individualized based on patient tolerance, anemia severity, and gestational stage. Similarly, outcome assessments varied, with haemoglobin and ferritin measured at different time points across studies from weekly monitoring to evaluations performed only at delivery. Such heterogeneity may have contributed to differences in pooled effect estimates and should be considered when interpreting these results.

From a clinical perspective, iron-deficiency anaemia during pregnancy is a treatable condition, and timely intervention is crucial. Current recommendations suggest that IV iron should be considered when oral supplementation or dietary measures are ineffective, poorly tolerated, or initiated late in gestation. While oral iron may take 3-6 months to restore iron stores, IV iron enables more rapid correction and is therefore preferred in the third trimester when time to delivery is limited. The 2017 NATA consensus further recommends IV iron for women who show no response to oral therapy within 2-4 weeks, present with severe anemia (Hb<8 g/dl), or are diagnosed with IDA after 34 weeks of gestation.[41]

Strengths and limitations

This systematic review offers several notable strengths. It represents the most current and comprehensive synthesis of evidence comparing oral and intravenous iron therapy in pregnant women, conducted using rigorous methodology aligned with PRISMA 2020 guidelines and the Cochrane handbook. However, certain limitations must be acknowledged. Firstly, not all included studies reported on all predefined outcomes, particularly fetal outcomes, which limited the ability to draw firm conclusions in this area.

Secondly, the methodological quality of studies varied in certain domains such as blinding and potential cultural biases of researchers the assessment was unclear, leaving room for bias. However, the overall judgment rated all studies as having a low risk of bias. Thirdly, the possibility of publication bias cannot be entirely ruled out for some outcomes, given the limited number of trials available. Additionally, several critical outcomes did not achieve statistical significance, partly due to wide confidence intervals and considerable heterogeneity among studies. Interestingly, outcomes with low heterogeneity generally showed no significant difference between intravenous and oral iron, suggesting that the two routes may be comparable for certain parameters. While the findings point to potential advantages of intravenous iron, their clinical applicability should be interpreted with caution due to variations in study design and outcome reporting.

Despite certain limitations, our findings strengthen the evidence supporting IV iron as a safe and effective alternative to oral supplementation in pregnancy, particularly in cases where rapid iron repletion is required or adherence to oral therapy is problematic. While oral iron remains suitable for mild anaemia or preventive use, IV iron should be prioritised for women with moderate to severe anaemia, intolerance to oral formulations, or those presenting later in pregnancy. However, further large-scale, high-quality trials are warranted to better define standardised dosing strategies, clarify long-term maternal and neonatal outcomes, and guide global clinical practice.

CONCLUSION

This meta-analysis demonstrates that intravenous iron therapy offers superior efficacy and better tolerability compared to oral iron supplementation in pregnant women with iron deficiency anaemia. Given the significant burden of maternal anaemia and its implications for both maternal and fetal outcomes, optimising iron repletion strategies is crucial. Future research should focus on long-term maternal-child health outcomes, cost-effectiveness of IV therapy in resource-limited settings, and standardised protocols for anaemia screening and management in pregnancy.

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